Does Agomelatine Have Antidepressant Action?

Michael Young, BIS¹, David Middlemas, Ph.D.²

¹ATSU-Kirksville College of Osteopathic Medicine, Kirksville, MO
²ATSU-Kirksville College of Osteopathic Medicine, Kirksville, MO

Background: Juvenile depression is becoming a prominent disorder with few antidepressant drugs that are effective. Agomelatine is a melatonin receptor agonist (M1, M2) and a serotonin receptor antagonist (5-HT2c). Agomelatine has been seen to positively affect adult humans and rats in treating the structural and behavioral changes that are characteristic of depression. The purpose of this project is to investigate the effects of agomelatine on hippocampal neurogenesis and behavior in juvenile rats.

Methods: Postnatal day 21 (PND21) juvenile rats were divided into 2 subgroups: 1) neurogenesis, 2) behavioral. Each subgroup was further divided into experimental and control groups and injected intraperitoneally (IP) with agomelatine (10 mg/kg) or 1% hydroxyethyl cellulose respectively. The neurogenesis subgroup was injected once a day for 14 days. The behavioral subgroup was injected for 3 days, the first 2 days according to a porsolt forced swim test protocol and once on the third day. The neurogenesis subgroup was also injected IP with BrdU three times a day for two days at the end, mitogenesis, or the beginning, cell survival, of the 14 day injection period. After BrdU administration the rats were sacrificed, and brain tissues fixed. The fixed brains were sectioned and analyzed using immunohistochemistry to detect BrdU and NeuN to assess differences in hippocampal neurogenesis. The behavioral subgroup was subjected to a porsolt forced swim test to detect antidepressant activity, an open field test to detect locomotor differences, and an elevated plus maze to detect anxiety differences.

Results: Preliminary results show behavioral and structural trends that may be characteristic of an antidepressant effect. The results of the forced swim test showed that agomelatine significantly decreased immobility time (p<0.05), which indicates a decrease in depressive-like behavior. The open field and elevated plus mazes showed no differences between groups. The immunohistochemistry analysis of mitogenesis showed an increased number of hippocampal cells in the subgranular cell layer (SGL), but no difference between groups in the hilus or in overall mitogenesis. The analysis of neurogenesis is underway.

Conclusion: Agomelatine may act as an antidepressant in juvenile rats and may be effective in treating juvenile depression.

Responsible Author: David Middlemas, Ph.D., dmiddlemas@atsu.edu; 660.626.2326

Key words: Agomelatine; Mitogenesis; Neurogenesis; Forced Swim Test